# INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 00/20008

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07H19/04 C12N9/10 A61K31/706 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07H C12N A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | WO 99 08110 A (SHEPARD H MICHAEL ;NEWBIOTICS INC (US)) 18 February 1999 (1999-02-18) | 1-3 |
| A | page 21 --- | 37 |
| X | GOODWIN ET AL: "Incorporation of alkylthiol chains at C-5 of deoxyuridine" TETRAHEDRON LETTERS,NL,ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 34, no. 35, 1993, pages 5549-5552, XP002123383 ISSN: 0040-4039 cited in the application page 5550, scheme I --- | 1-3 |

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

| Date of the actual completion of the international search | Date of mailing of the international search report |
|---|---|
| 23 October 2000 | 12.01 |

| Name and mailing address of the ISA | Authorized officer |
|---|---|
| European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016 | de Nooy, A |

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | ROBINS M J ET AL: "NUCLEIC ACID RELATED COMPOUNDS. 39. EFFICIENT CONVERSION OF 5-IODO TO 5-ALKYNYL AND DERIVED 5-SUBSTITUTED URACIL BASES AND NUCLEOSIDES" JOURNAL OF ORGANIC CHEMISTRY,US,AMERICAN CHEMICAL SOCIETY. EASTON, vol. 48, no. 11, 1983, pages 1854-1862, XP002069924 ISSN: 0022-3263 cited in the application page 1855-1856, all structures | 1-3,5 |
| X | DE CLERCQ ET AL: "Antiviral activity of novel deoxyuridine derivatives" CURRENT CHEMOTHERAPY: PROCEEDINGS OF THE INTERNATIONAL CONGRESS OF CHEMOTHERAPY, vol. 1, no. 1, 18 September 1978 (1978-09-18), pages 352-354, XP002094189 page 353, figure 1 | 1-3 |
| X | BUDAVARI (ED.): "The Merck index" 1996 , MERCK & CO., INC. , WHITEHOUSE STATION, NJ XP002147030 3493. Doxifluridine. | 1-3 |
| X | BUDAVARI (ED.): "The Merck index" 1996 , MERCK & CO., INC. , WHITEHOUSE STATION, NJ XP002148607 4148. Floxuridine. | 1-3 |
| X | BUDAVARI (ED.): "The Merck index" 1996 , MERCK & CO., INC. , WHITEHOUSE STATION, NJ XP002148608 4934. Idoxuridine. | 1-3 |
| X | CLERCQ DE E: "ANTIVIRAL ACTIVITY SPECTRUM AND TARGET OF ACTION OF DIFFERENT CLASSES OF NUCLEOSIDE ANALOGUES" NUCLEOSIDES & NUCLEOTIDES,US,DEKKER, NEW YORK,NY,, vol. 13, no. 687, 1994, pages 1271-1295, XP000579320 ISSN: 0732-8311 page 1281 | 1-3,5 |

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# INTERNATIONAL SEARCH REPORT

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-3 (in part)

Present claim 1 contains a substituent bearing a R15 group which is not defined in the application. A lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claim impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely substituents not bearing a R15 group.

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty of claims 1-3. So many documents were retrieved that it is impossible to determine which parts of the claims may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT).
For these reasons, it appears impossible to execute a meaningful search and/or to issue a complete search report over the whole breadth of the above mentioned claims. The search report for those claims can only be considered complete for the one or two halogen containing compounds mentioned in examples 12-16 of the application.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-11 (in part), 13 (in part), 14 (in full), 15 (in part), 16 (in full), 17 (in part), 18-20 (in full), 25-30 (in full), 32 (in part), 35-52 (in part)

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end(s) (e.g. as R4 in claim 1) or consists of a total of one or two halogenides (F, Cl, Br, I).

2. Claims: 1-11 (in part), 13 (in part), 15 (in part), 17 (in part), 35-52 (in part).

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end(s) (e.g. as R4 in claim 1) or consists of a total of one or two CN groups.

3. Claims: 1-11 (in part), 35-36 (in part).

A compound containing a modified pyrimidine base and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a total of a SO3H group.

4. Claims: 1-11 (in part), 21 (in full), 31 (in full), 35-52 (in part)

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a CO2H or a CO2CH2CH3 or a CO2CH3 or a CO2R9 group where R9 is a lower straight or branched chain alkyl.

5. Claims: 1-11 (in part), 23 (in full), 35-52 (in part).

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|---|---|---|
| X | D.E. BERGSTROM: "Synthesis of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deox yuridine and related analogues: potent and unusually selective antiviral activity of (E)-5-(3,3,3-trifluoro-1-propenyl)-2'-deox yuridine against Herpes Simplex virus type 1" J. MED. CHEM., vol. 27, 1984, pages 279-284, XP002147028 cited in the application page 279, structures 4-6 --- | 1-3,5 |
| X | T.W. ABRAHAM ET AL.: "Synthesis and biological activity of aromatic amino acid phosphoramidates of 5-fluoro-2'-deoxyuridine and 1-beta-arabinofuranosylcytosine: evidence of phosphoramidase activity" J. MED. CHEM., vol. 39, 1996, pages 4569-4575, XP002147029 cited in the application page 4570, scheme 1 --- | 1-3 |
| A | WO 99 23104 A (ANDERSON LAWRENCE ;KATKI ASPANDIAR G (US); KLECKER RAYMOND W (US);) 14 May 1999 (1999-05-14) claims --- | 1,37 |
| P,X | WO 99 37753 A (GROZIAK MICHAEL P ;SHEPARD H MICHAEL (US); NEWBIOTICS INC (US)) 29 July 1999 (1999-07-29) the whole document ----- | 1-52 |

# INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/20008

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [ ] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. [X] Claims Nos.: 1-3 (in part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [X] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-11,13,15,17,32,35-52(all in part); 14,16,18-20,25-30(all completely)

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a Si(CH3)3 group.

6. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a CHO group.

7. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a NO2 group.

8. Claims: 1-11 (in part), 34 (in full), 35-52 (in part)

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a CF3 or a CCl3 group.

9. Claims: 1-11 (in part), 12 (in full), 35-36 (in part)

A compound containing a modified pyrimidine base, a pharmaceutical composition containing this compound and a use of the compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a phosphoramidate group as depicted at page 2 of claim 1.

10. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -O-NH-C(O)-NH2 group.

11. Claims: 1-11 (in part), 35-36 (in part)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -Z-CH2-CH(NH-C(O)-CH2)-CH(OH)-CH=CH-(CH2)12CH3 group as depicted at page 2 of claim 1 and where Z is as defined in claim 1.

12. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -Z-CF2-CH2-CHF-CO2H or a -Z-CF2-CHF-CH2-CO2H or a -Z-CF2-CH2-CO2H or a -Z-CF2-CH(CH3)-CO2H group as depicted at page 2 of claim 1 where Z is as defined in claim 1.

13. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -Z-CF2-C(YaYbYc) group as depicted on page 2 of claim 1 where Z, Ya, Yb and Yc are as defined in claim 1.

14. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -Z-CF2-CH2-CH2-NO2 group where Z is as defined in claim 1.

15. Claims: 1-11 (in part), 35-36 (in part)

A compound containing a modified pyrimidine base, and a pharmaceutical composition containing this compound, where the substituent in the 5-position (the position defined as in claim 1) of the base is bearing at its end (e.g. as R4 in claim 1) or consists of a -Z-C6H4-NO2 group as depicted on page 2 of claim 1 where Z is as defined in claim 1.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 00/20008

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|---|---|---|---|
| WO 9908110 A | 18-02-1999 | AU 9016998 A | 01-03-1999 |
| | | CN 1265741 T | 06-09-2000 |
| | | EP 1004022 A | 31-05-2000 |
| WO 9923104 A | 14-05-1999 | AU 1449599 A | 24-05-1999 |
| | | EP 1027365 A | 16-08-2000 |
| WO 9937753 A | 29-07-1999 | AU 2464699 A | 09-08-1999 |
| | | BR 9907736 A | 17-10-2000 |
| | | EP 1045897 A | 25-10-2000 |